



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/463,904	06/05/1995	JOSEPH B. PHIPPS	ALZ0006-00	9244
48394	7590	07/01/2008		
DIEHL SERVILLA LLC 77 BRANT AVE SUITE 210 CLARK, NJ 07066			EXAMINER BOCKELMAN, MARK	
			ART UNIT 3766	PAPER NUMBER
			NOTIFICATION DATE 07/01/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docket@dsiplaw.com
skahaly@dsiplaw.com
jescobar@dsiplaw.com

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOSEPH B. PHIPPS

Appeal 2007-1556
Application 08/463,904
Technology Center 3700

Decided: June 27, 2008

Before DONALD E. ADAMS, RICHARD M. LEBOVITZ, and JEFFREY
N. FREDMAN, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal from the final rejection of claims 1, 4, and 7-9. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

The claims are drawn to a method of delivering “fentanyl salts through a body surface by iontophoresis from a delivery device.” The concentration of fentanyl salt in the device is claimed to be “above 16

mM . . . substantially throughout the . . . [drug] delivery period.” Fentanyl is a synthetic opiate utilized for pain management; its delivery by electrotransport (which includes iontophoresis) had been described in the prior art (Spec. 5: 21 to 6: 26).

Appellant appeals from the final rejection of claims 1, 4, and 7-9, which are all the pending claims. The following rejections are on review in this appeal:

1) Claims 1, 4, and 7-9 under 35 U.S.C. § 103 as obvious over Phipps ‘739 (U.S. Pat. No. 5,423,739, issued Jun. 13, 1995) in view of Rebinder (Chapter 12, Iontophoresis, in *Electrokinetischeskie kapillarnykh system: monographicheskies sbbrnik*, Editor: Rebinder, Moskow USSR Academy of Science, 1956, pp. 310-327; translation presented as pp. 1-31), Phipps ‘894 (U.S. Pat. No. 5,125,894, issued Jun. 30, 1992), and Muller (U.S. Pat. No. 5,320,731, issued Jun. 14, 1994) (Ans. 5);

2) Claims 1, 4, and 7-9 under 35 U.S.C. § 102(b) as anticipated by Haak (U.S. Pat. No. 5,203,768, issued Apr. 20, 1993), or in the alternative, under 35 U.S.C. § 103(a) as obvious over Haak in view of Rebinder, Phipps ‘894, Muller, or in view of Newman (U.S. Pat. No. 4,931,046, issued Jun. 5, 1990) (Ans. 13);

3) Claims 1, 4, and 7-9 under 35 U.S.C. § 102(b) as anticipated by Theeuwes (U.S. Pat. No. 5,232,438, issued Aug. 3, 1993), or in the alternative, under 35 U.S.C. § 103(a) as obvious over Theeuwes in view of Rebinder, Phipps ‘894, Muller, or in view of Newman (Ans. 15).

4) Claims 1, 4, and 7-9 under the judicially created doctrine of double-patenting as obvious over Claims 1-9 of Southam (U.S. Pat. No. 6,171,294 B1, issued Jan. 9, 2001) (Ans. 16).

We select claims 1 and 9, which read as follows, as representative of the claimed subject matter:

1. In a method of delivering an analgesic drug selected from the group consisting of fentanyl salts through a body surface by iontophoresis from a delivery device having a donor reservoir containing an at least partially aqueous solution of a fentanyl salt, the improvement comprising maintaining the concentration of the salt in solution above a level at which the iontophoretic flux of the drug is dependent on the concentration of the drug salt in the solution, said level of said fentanyl salt being above about 16 mM, the concentration of the salt in the solution being maintained substantially throughout the total analgesic drug iontophoretic delivery period wherein the analgesic drug is delivered through the body surface.

9. The method of claim 1, wherein the iontophoretic flux of the analgesic drug is substantially proportional to a level of current applied by the delivery device during the iontophoretic drug delivery.

OBVIOUSNESS OVER PHIPPS ‘739

Claims 1, 4, and 7-9 stand rejected under 35 U.S.C. §103 as obvious over Phipps ‘739 in view of Rebinder, Phipps, ‘894, and Muller (Ans. 5).

Issue

Claim 1 is directed to a method of delivering a fentanyl salt from a delivery device through a body surface by iontophoresis. The concentration of fentanyl salt in the device is claimed to be “above 16 mM . . . substantially throughout the . . . [drug] delivery period.”

The Examiner contends that it would have been routine in the prior art to have optimized the fentanyl salt above a threshold concentration, i.e., the claimed concentration, to deliver predictable amounts of the fentanyl drug

(Ans. 11). Appellant contends that drug flux across the skin is independent of its concentration over a broad range and thus it would not have been obvious to have selected a fentanyl salt concentration as high as 16 mM (App. Br. 25-26).

The issue in this appeal is whether the Examiner erred in finding that the claimed fentanyl concentration in a drug delivery device would have been obvious to persons of ordinary skill in the art.

Scope and content of the prior art

1.¹ Claim 1 “is written in the form of a Jepson type claim” where “the preamble of the claim indicates that the delivery of fentanyl salt by iontophoresis is known and admitted prior” (Ans. 5).

The Phipps ‘739 patent

2. Phipps ‘739 teaches iontophoresis for delivering drugs across the skin (Phipps ‘739, Abstract; Ans. 5).

3. Fentanyl is among a list of active agents that Phipps ‘739 describes as suitable for iontophoretic delivery (Phipps ‘739, at col. 13, l. 50; Ans. 5).

4. Phipps ‘739 does not teach the concentration of fentanyl that is used to achieve analgesic effects (Ans. 6).

Rebinder

5. Rebinder describes the results of quantitative studies involving the movement of drugs by iontophoresis across membranes.

6. According to theoretical equations, Rebinder states that “the amount of substance introduced, is completely governed by the parameters of the internal solution and the skin tissues, and does not depend on the

¹ Numbered findings of fact (FF).

concentration of the medicinal substance used for iontophoresis” (Rebinder, at 12).

7. However, Rebinder acknowledges that

[p]ublished experimental data on this question [concentration independence] are inconsistent. On the one hand, qualitative clinical observations suggest that under the conditions of clinical practice, the higher the concentration of the initial solution, the greater the therapeutic effect. These data are largely based on the iontophoresis of complex organic ions. On the other hand, the quantitative data of Schafferstein (1939) show that for a number of simple ions, tenfold changes in the concentration of a substance have practically no effect on the amount introduced within the limits of experimental error.

(Rebinder, at 13; *see* Ans. 8.)

8. To address this issue, Rebinder performed experiments on model membranes and found:

Amount of the dye [as a model for a drug] introduced per coulomb (p/q) does not depend on the concentration of the starting dye solution . . . , the duration of the experiment, or the strength of density of the current.

(Rebinder, at 19.)

9. Rebinder also found that a “parasitical ion” added to the dye solution had no effect on the amount of dye introduced across the model membrane when a *small* amount of ion was added to a *high* concentration of dye (Rebinder, at 20; at 19, Table 118).

10. However, when the parasitical ion was added to a *dilute* dye solution, “a reduction in the amount of major [dye] ion introduced” across the membrane was observed (Rebinder, at 20; at 19, Table 118).

11. In other words, “the amount of drug delivered is independent of concentration, however, the presence of parasitic ions, in sufficient amounts

relative to the major ion, may reduce the efficiency of the major ion delivery” (Ans. 8).

12. Additional experiments conducted on living skin by Rebinder showed that amount of drug transported across the skin “does not depend” on its concentration in the external solution (Rebinder, at 29).

13. However, Rebinder asks “how can these experimental results, which also have a theoretical explanation, be squared with the increase in the therapeutic effect observed with increasing [drug] concentration” in the external solution applied to the skin (Rebinder, at 29).

14. Rebinder explains that the “most important reason for the discrepancy” is the presence of parasitical ions in the external drug solution (Rebinder, at 29).

15. “It is perfectly clear that in the presence of parasitic ions, the medicinal substance will be introduced in smaller amounts . . . and the lower the concentration of the solution, the less introduced” (Rebinder, at 29).

16. Based on Rebinder’s teaching, persons of ordinary skill in the art would have known that “the relative amount of parasitic ions to major ions effects [sic, affects] the delivery rate of simple as well as complex ions . . . [and] the delivery of complex organic ions may involve other factors and generally produce a fall off as . . . the ratio of major ions to parasitic ions (i.e. complex ion concentration) gets smaller” (Ans. 9-10).

Phipps ‘894 patent

17. Phipps ‘894 makes the following statements:

[O]ver a sustained period of time, for a typical iontophoretic system with little or no extraneous ions, constant rate of target ion delivery or transport can be maintained with a lowering of voltage, at least over a given range of concentrations of drug

ion in the active reservoir, wherein the concentration is not modified greatly and *is above a threshold level* determined by physical/chemical properties of the transported species and tissue through which transport occurs. With respect to this threshold level, reference is made to the principles described in the next section herein.

(Phipps '894, at cols. 10, l. 62 to 11. 5.) (Emphasis added.)

18.

2. The Effect of Concentration of Drug Ions on Rate of Drug Delivery at Constant Current

In general, although rate of drug delivery is proportional to current, at a constant current the rate of drug delivery (R_d) is independent of drug concentration (i.e. target species concentration) in the active electrode reservoir, *provided that the concentration is at least above a threshold level (and little or no extraneous ions are present)*; see Padmanabhan, R. V. et al. *J. Controlled Release*, supra.

(Phipps '894, at col. 11, ll. 6-16.) (Emphasis added.)

19. Phipps '894 at columns 11-14 describes the effect of extraneous ions in the drug reservoir.

20. The “extraneous ions” are the same as the “parasitical ions” described in Rebinder.

21. According to Phipps '894, extraneous ions when present in the drug reservoir “have a profound significant effect” on the principles stated in the previous sections (i.e., FF 17-18).

22. “A general principle . . . is that: if the active electrode reservoir includes therein both a charged target [drug] species and extraneous ions [of the same charge]; and, if the target species and extraneous ions do not possess identical mobilities, in time, under a given applied voltage (i.e.,

galvanostatic conditions), the rate of delivery of the target species will change” (Phipps ‘894, at col. 12, ll. 61-67).

23. Thus, in the presence of extraneous (parasitical) ions, the rate of delivery of a drug species changes and is not independent of its concentration – as it is in the absence of such ions.

Muller patent

24. Muller describes a device for administration of drugs across the skin by iontophoresis (Muller, at col. 1, ll. 7-9).

25. Muller states that in the presence of “ions other than those of the active principle” [the drug species] it is “preferable . . . for the quantity of active principle present in the reservoir element at the start of the operation to be in excess with respect to the said given total quantity, the said excess being able, for example, to be from approximately 2% to 1000% and more specifically from approximately 2% to 500% of this given total quantity” to be administered to the subject (Muller, at col. 3, ll. 56-65; *see* Ans. 12).

Reason to combine the prior art

26. The Examiner finds that it “was . . . known at the time of applicant’s invention that in order to deliver a desired quantity of medicament to a pat[i]ent, excess quantities must be provided [FF 9, 10, 25] so as to negate the effects of competing ions since efficiency decreases as drug delivery ions are depleted in the reservoir [FF 11, 16]” (Ans. 12-13).

27. “It was also recognized that a threshold value exists wherein the effects of competing ions are no longer felt and that the amount of drug delivered become strictly dependent on the amount of current applied” (Ans. 12-13; *see* FF 17, 18).

28. Thus, persons of skill in the art would have had reason to determine an optimal concentration of fentanyl to use “in an iontophoresis patch and to perform the routine testing of determining the most safe and effective concentrations of drug in the reservoirs to achieve patient analgesia” (Ans. 13).

Analysis

During examination, the Examiner bears the initial burden of establishing a prima facie case of obviousness. *In re Kumar*, 418 F.3d 1361, 1366 (Fed. Cir. 2005). In making an obviousness determination, a reason must be provided as to why persons of ordinary skill in the art would have combined the prior art to have arrived at the claimed invention. *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

After reviewing the scope and content of the prior art and the reason for combining it, it is our opinion that prima facie obviousness of the subject matter of claim 1 has been established.

By claiming the invention in “Jepson format”, Appellant admits that administration of fentanyl by iontophoresis was known in the art (FF 1).² The difference between the admitted prior art and the claimed invention is that claim 1 requires the concentration of fentanyl salt to be above “about 16 mM”, “above a level at which the iontophoretic flux of the drug is dependent on the concentration of the drug salt in the solution.” The claim also

² “Drafting a claim in Jepson format (i.e., the format described in 37 CFR 1.75(e); see MPEP § 608.01(m)) is taken as an implied admission that the subject matter of the preamble is the prior art work of another. *In re Fout*, 675 F.2d 297, 301 213 USPQ 532, 534 (CCPA 1982) (holding preamble of *Jepson*-type claim to be admitted prior art where applicant's specification credited another as the inventor of the subject matter of the preamble).” M.P.E.P. 2129, 8th Edition, Revision 5, September 2007.

requires that the fentanyl salt concentration is “maintained substantially throughout the total analgesic drug iontophoretic delivery period.”

The Examiner contends that such amount would have been routinely determined based on the suggestion in the prior art that a threshold drug concentration is necessary to eliminate the effects of competing parasitical ions (FF 26-28). We agree with the Examiner’s findings and reasoning, and thus turn to Appellant’s rebuttal evidence and arguments.

Appellant argues that the claimed concentration of fentanyl would not have been obvious because “there is no dependence of the amount of drug introduced on the concentration of drug used for iontophoresis and there is no dependence on the amount introduced per coulomb (p/q) on strength or duration” (App. Br. 23). Appellant asserts that the influence of “parasitic ions . . . has nothing to do with the present invention” (*id.* at 24). They assert that Phipps ‘894 shows that “even with a drug concentration [of hydrocodone] as low as 10 mM, the average steady state rate is approximately the same as it is at 800 mM” (*id.* at 25). To support the position that drug delivery is independent of drug concentration, they rely on the Phipps I and II Declarations (Declarations under 37 C.F.R. § 1.132, dated June 6, 1997 and August 3, 1998, respectively), the Padmanabhan publication, and the Kasting publication (App. Br. 24-26).

We have considered this rebuttal evidence, but are not persuaded by it that the Examiner erred.

Table 2 of Phipps ‘894 is stated to show that the “the average rate of delivery (microgram per hour) [for an aqueous hydromorphone HCl solution] was relatively constant, regardless of drug concentration” (Phipps ‘894, at col. 37, ll. 4-10). However, this experiment is not described to have

been conducted in the presence of extraneous cations (Phipps' 894, beginning at col. 36, l. 10) as there were in Rebinder's experiments (FF 10). Nonetheless, Phipps '894 characterizes this example as illustrating "independence of drug delivery rate . . . *above a threshold concentration*" (Phipps '894, at col. 36, ll. 10-15) (emphasis added) – consistent with the Examiner's position.

Furthermore, Experiment 1 of Phipps '894 – which contains extraneous cations (Phipps '894, at col. 35, Table 1, "Na", "K", "Mg", "Ca") – shows increasing delivery rate of the hydrocodone (*id.* at col. 35, ll. 5-10; Fig. 1), also consistent with the Examiner's argument about the influence of extraneous ions on delivery rate.

Dr. Phipps in the Phipps II Declaration refers to the "Kasting model" (Phipps II Declaration 5). Dr. Phipps describes this model in the Phipps I Declaration:

An often cited reference for the theoretical basis of electrotransport is the publication of G.B. Kasting and J.C. Keister . . . The authors make theoretical predictions of the effect of donor drug concentration on drug delivery efficiency (i.e., rate of drug delivery per unit current) for several cases. Their Case 1, beginning on page 202 develops the theoretical prediction for a drug salt with no added NaCl in the donor reservoir and normal saline on the receptor side of the in vitro cell. On page 204, they conclude that, for this case:

... the efficiency of drug delivery is largely determined by the ratio of drug diffusivity in the skin to that of the predominant counterion on the opposite side of the membrane. It is independent of drug concentration in this example.

(Phipps I Declaration 3-4.) (Emphasis added.)

Of course, Case I was accomplished in the absence of extraneous ions (“no added NaCl”). However, Kasting also describes a “Case 2” which is characterized as having normal saline, i.e., extraneous sodium cations, in the drug phase (Kasting, at 205, col. 2). Kasting states that under these conditions the “drug transference number . . . is now a strong function of concentration, since the drug competes with Na^+ on the donor side as well as with Cl^- on the receptor side” (*id.*). Kasting also states that “[e]fficient drug delivery is possible only if the concentration is kept high and the value of the drug diffusivity . . . is not too low” (*id.*). Thus, contrary to Dr. Phipp’s statements, Kasting appears to support the Examiner’s position.

Dr. Phipps also states that the Padmanabhan publication concludes that “due to the mobility of the ions in the solution, the rate limiting feature is the transport through the skin and not the concentration in the donor reservoir” (Phipps II Declaration 3).

We do not find this argument persuasive. Padmanabhan’s experiments appear to have been conducted in the absence of extraneous cations; thus, the conclusions in this paper are not necessarily applicable to Rebinder’s experiments which were carried out in the presence of competing extraneous cations.

It is also stated in the Phipps II declaration that “the Examiner has seemingly failed to appreciate the role of extraneous ions on the threshold concentration concept” (Phipps II Declaration 4). Dr. Phipps asserts that “because small excipient ions (like Na^+ and K^+) are much more mobile in the solution and skin than fentanyl and are typically present in an amount less than the amount of drug ions, they are typically depleted during the first part of the treatment” (*id.* at 5).

Firstly, we note that the claims do not require either the presence or absence of extraneous ions – and are clearly open as to the amount. Thus, Dr. Phipps’ statement that the ions are “typically present in an amount less than the amount of drug ions” is not persuasive because the claim is not limited to “typical” amounts. Secondly, it is not clear from Dr. Phipps’ declaration how the Examiner has “failed to appreciate the role of extraneous ions on the threshold concentration concept.” It seems clear that Phipps ‘849 expressly teaches that a threshold would exist; the Examiner provides a logical explanation as to how extraneous ions would influence the threshold – citing Rebinder as evidence. We do not see a defect in the Examiner’s reasoning.

In the Reply Brief, Appellant states that it “is well known in the art of iontophoresis that as the iontophoretic flux of drug decreases, a greater portion of electrotransport current is carried by chloride ions migrating from the other side of the epidermis, and not due to the presence of extraneous ions as stated by the [E]xaminer” (Reply Br. 11). Appellant states “[t]his fact is supported by an article authored by the inventor . . . in a peer-reviewed article published in the Journal of Pharmaceutical Sciences in May of 1989”³ (*id.*) That publication, as quoted by Appellant, expressly states that ““the extraneous ion concentration in the donor reservoir should be minimized in order to maximize the delivery efficiency.’ (emphasis supplied)” (Reply Br. 12). The claims do not require a minimal concentration of extraneous ions; thus, Appellant is attempting to distinguish the prior art over a limitation that does not appear in the claims. Moreover,

³ Appellant does not list the full citation of the article in the Reply Brief.

the statement that the extraneous ions “should be minimized” appears to support the Examiner’s argument that extraneous ions influence the delivery of the drug. Appellant does not explain how chloride ions migrating from the donor side would eliminate the extraneous ion effect. Once again, we find that the evidence favors the Examiner’s position.

Appellant also argues that, because of its toxicity and potential for abuse, persons of skill in the art would not have utilized concentrations of fentanyl as high as 16 mM as are present in the claimed delivery device (App. Br. 2-4; Phipps I Declaration 2.

We are not convinced by this argument that the Examiner erred. Considerations about the safety of a medical device are entertained by the Food and Drug Administration (FDA), not the Patent and Trademark Office. *See In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995). In this case, while there could conceivably be public health and safety considerations that would discourage high fentanyl concentrations in a medical device, we do not agree that such considerations come into play when *obviousness* is at issue and there is no evidence that the suggested concentrations would not work. The prior art clearly suggests a device loaded with the claimed fentanyl concentration; whether such device would be approved or marketed to the public is another question unrelated to its patentability.

As stated in *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992): “[T]he examiner bears the initial burden . . . of presenting a prima facie case of unpatentability. . . . After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.” In this case, after considering all the evidence

of record, we conclude that the Examiner's position is supported by the preponderance of the evidence. Consequently, we affirm the rejection of claim 1. Claims 4, 7, and 8 fall with claim 1 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii).

Claim 9

Claim 9 is directed to the method of claim 1, where “the iontophoretic flux of the analgesic drug is substantially proportional to a level of a current applied by the delivery device during the iontophoretic drug delivery.”

Phipps '894 states that the “rate of drug delivery is proportional to current” (FF 18) – leading to the reasonable expectation that the “flux” would be “substantially proportional to a level of a current” as required by claim 9.

Appellant argues that “as illustrated in Figure 2 [of the Specification], once the concentration of fentanyl falls below the defined level, which is the result of fentanyl being depleted from the reservoir, the iontophoretic flux significantly decreases and is no longer substantially proportional to the level of iontophoretic current applied during drug delivery” (App. Br. 36).

This argument is not persuasive. We have already concluded above that it would have been obvious to persons of ordinary skill in the art to choose a threshold concentration of fentanyl to maintain a predictable rate of delivery. As taught by Phipps '894, it would be expected that, above this threshold, drug flux would be proportional to current (FF 18).

ANTICIPATION AND OBVIOUSNESS OVER HAAK

Claims 1, 4, and 7-9 stand rejected under 35 U.S.C. § 102(b) as anticipated by Haak, or in the alternative, under 35 U.S.C. § 103(a) as

obvious over Haak in view of Rebinder, Phipps '894, Muller, or in view of Newman (Ans. 13).

Anticipation over the Haak patent

Findings of Fact

29. Haak describes a therapeutic system to transdermally deliver fentanyl (Haak, at col. 13, l. 50 to col. 14, l. 53).
30. The drug reservoir comprises fentanyl HCl (Haak, at col. 13, l. 50 to col. 14, l. 3).
31. When the device is activated, at a current of 0.6 mA, it delivers about 25 µg of fentanyl over a period of five minutes (Haak, at col. 14, ll. 19-23; Ans. 13).
32. “The device is designed with an on off switch or a controller that automatically turns the device on and off as the pain medicament is needed (column 10 lines 44-54) or may be on a timer so that a known amount (column 14 lines 20-23) is delivered each time it is activated. One on-off cycle meets the claim language if the device stays above the 16mM concentration” (Ans. 13).
33. “Haak et al teaches that a predetermined constant level of current delivers the drug at a constant rate (column 10 line 54 -59)” and that current controls the amount of drug delivered (Ans. 13; Haak, at col. 4, ll. 25-30).
34. The Examiner states that for the device to deliver drug linearly at a constant rate each time it is activated, “it is inherent that the concentration is in the range” which is claimed (Ans. 13-14).

Analysis

The PTO does not have the ability “to manufacture products or to obtain and compare prior art products.” *In re Best*, 562 F.2d 1252, 1255

(CCPA 1977). Thus, once “the PTO shows sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d 705, 708 (Fed. Cir. 1990).

In this case, the Examiner provides a logical reason for believing that Haak describes a drug delivery device that meets all the limitations of claim 1 (FF 29-34). Thus, we turn to Appellant’s rebuttal arguments and evidence.

Appellant contends that the “Examiner’s position ignores the fact that Haak, et al. does not state that the device is to be operated for a total of only one hour. . . . The patent example does not provide the total period of operation and is silent about the delivery rate . . . In view of the disclosed presence of three lithium batteries in the Example (column 14, lines 14- 15), there is nothing to dispute the possibility that the device can operate for a substantial period of time, such as until the reservoir is depleted” (App. Br. 31).

This argument is not persuasive. Claim 1 does not require the delivery device to be operated until is “depleted” or “for a substantial period of time” as argued by Appellant. The claim recites that the salt concentration is “maintained substantially” above 16 mM “throughout the total . . . delivery period”, but does not positively recite the delivery period’s duration. Accordingly, we agree with the Examiner that this limitation is met by one on-off cycle (FF 32). Appellant does not otherwise provide evidence that the fentanyl concentration disclosed in Haak’s delivery device does not meet the claimed limitation. Consequently, we affirm the rejection of claim 1. Claims 4, 7, and 8 fall with claim 1 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii).

As to claim 9, Haak teaches that the amount of drug delivery can be controlled by current (FF 33). Thus, we affirm the rejection of claim 9.

Obviousness over Haak in view of Rebinder, Phipps '894, and Muller

The Examiner contends that Haak in view of Rebinder, Phipps '894, and Muller suggests the claimed invention for the same reasons as described above for Phipps '739 in combination with the same cited references (Ans. 14-15). Appellant argues as he did for the obviousness rejection over Phipps '739. We did not find these arguments persuasive as to Phipps '739 and do not find them persuasive as applied to Haak for the reasons set forth above. Accordingly, we affirm the rejection of claims 1 and 9. Claims 4, 7, and 8 fall with claims 1 and 9 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii).

Obviousness over Haak in view of Newman

The Examiner contends that “it would have been obvious in view of Newman . . . to have placed as much drug as desired into the Haak et al. device and limit the amount delivered by a control circuit so that the patient may undergo self treatment for days on end as in the teaching of Newman. . . .To have implemented such a system with the Newman teachings device would mean providing high concentrations fentanyl so as to provide multiple dosages of pain killing medication in a manner that assures a given amount of current delivers a given amount of drug as was long recognized as a requirement” (Ans. 15).

We have already affirmed the rejection of claims 1, 4, and 7-9 over Haak. Having found the claims anticipated by Haak, we agree with the

Examiner that the claims would also be obvious over Haak in combination with Newman since anticipation is the epitome of obviousness. See, e.g., *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1548 (Fed. Cir. 1983); *In re Fracalossi*, 681 F.2d 792, 794 (CCPA 1982); *In re Pearson*, 494 F.2d 1399, 1402 (CCPA 1974).

ANTICIPATION AND OBVIOUSNES OVER THEEUWES

Claims 1, 4, and 7-9 stand rejected under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 35 U.S.C. § 103(a) as obvious over Theeuwes in view of Rebinder, Phipps '894, Muller, or in view of Newman (Ans. 15).

Anticipation over Theeuwes

Findings of Fact

35. Theeuwes describes an electrotransport delivery system that can be used to administer fentanyl across the skin (Theeuwes, at col. 10, l. 26; Ans. 15).

36. The Examiner contends that “the recited concentrations in the applicant’s pending claims” are “inherent” in Theeuwes “for had the reservoir contained” a “concentration less than the requisite 16 mM, the amount actually delivered would have been less than Theeuwes et al calculated and the results of the claimed invention would not have been yielded” (Ans. 15-16).

Analysis

A “prior art reference may anticipate without disclosing a feature of the claimed invention if that missing characteristic is necessarily present, or inherent, in the single anticipating reference.” *SmithKline Beecham Corp. v. Apotex Corp.*, 403 F.3d 1331, 1343 (Fed. Cir. 2005). Once “the PTO shows

sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not.” *In re Spada*, 911 F.2d at 708.

In this case, the Examiner has not presented evidence that Theeuwes describes a delivery device in which the concentration of fentanyl salt in the device is “above 16 mM . . . substantially throughout the . . . [drug] delivery the period.” The Examiner states that the claimed concentration is inherent to Theeuwes device (FF 36), but does not point to any examples in which fentanyl is administered nor does he point to any guidance in Theeuwes in how to choose suitable fentanyl concentrations. We reverse the rejections of claims 1, 4, and 7-9 as anticipated by Theeuwes.

Obviousness over Theeuwes in view of Rebinder, Phipps '894, Muller

Findings of Fact

37. Theeuwes describes an equation (11) for flux across a membrane that is a function of drug concentration and the diffusion coefficient of the drug (Theeuwes, at col. 7, ll. 25-30).

38. Theeuwes states that equation (11) “indicates that it may be advantageous to operate at low donor drug concentration” (Theeuwes, at col. 7, ll. 44-45).

39. Theeuwes also states that “reducing the donor drug concentration will only increase” the flux ratio “if the transference number of the drug through the resin is high. Equation (11) also suggests a convenient means of characterizing membranes comprised of various materials since the” flux “ratio is predicted to be inversely proportional to the resin loading” (Theeuwes, at col. 7, ll. 51-56).

Analysis

The Examiner contends that Theeuwes in view of Rebinder, Phipps '894, and Muller suggests the claimed invention for the same reasons as described above for Phipps '739 in combination with the same cited references (Ans. 16).

Appellant contends that Theeuwes suggests “that it may be advantageous to operate at a low donor drug concentration depending on certain characteristics of the membrane. Accordingly, such passage would tend to counsel away from invention, particularly in light of the known characteristics of fentanyl” (App. Br. 34).

This argument is not persuasive. Appellant acknowledges that “certain characteristics of the membrane” determine whether low donor concentration would be advantageous in the Theeuwes system (*id.*). The instant claims, however, are not limited to a membrane type; thus, Appellant argues a limitation that is not recited in the claims.

In addition to this, Appellant contends that low concentrations would be advantageous in the Theeuwes system “particularly in light of the known characteristics of fentanyl” (*id.*). However, Appellant does not identify what characteristic of fentanyl would make low concentrations desirable in Theeuwes’s system. Thus, this argument is not supported by evidence and accordingly is not persuasive.

Finally, we note that the Examiner did not cite Theeuwes for its teaching of the relationship between a membrane’s characteristics and a suitable concentration of fentanyl. Rather, it was relied upon for its disclosure that fentanyl can be administered iontophoretically.

We affirm the rejections of claims 1 and 9 for the same reasons as for the obviousness rejection over Phipps '739 in view of Rebinder, Phipps '894, and Muller. Claims 4, 7, and 8 fall with claims 1 and 9 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii).

Obviousness over Theeuwes in view of Newman

The Examiner has the burden of establishing prima facie obviousness. Having found Theeuwes alone deficient, we further conclude that the Examiner has not provided sufficient evidence that it would have been obvious from the teachings of Theeuwes and Newman to make a delivery device with the claimed concentration of fentanyl. We reverse the rejection of claim 1, 4-7, and 9 as obvious over Theeuwes and Newman.

OBVIOUS-TYPE DOUBLE-PATENTING OVER SOUTHAM

Claims 1, 4, and 7-9 stand rejected under the judicially created doctrine of double-patenting as obvious over Claims 1-9 of Southam (Ans. 16).

Findings of Fact

Southam Patent

40. Claims 1, 2, 3, 6, and 7 of the Southam patent are reproduced below:

1. A method of obtaining self-administered analgesia in a human patient who is suffering from pain consisting of transdermally delivering solely by electrotransport a dose of about 20 µg to about 60 µg of fentanyl over a predetermined delivery period of up to about 20 minutes from an electrotransport device which includes a donor reservoir hydrogel formulation comprised of fentanyl, terminating said

delivery at the end of said delivery period and allowing the patient to self-administer from about 10 to about 100 additional of said doses over a period of 24 hours.

2. The method of claim 1, wherein about 35 μg to about 45 μg of fentanyl is delivered over a delivery period of about 5 to 15 minutes.

3. The method of claim 1, wherein about 40 μg of fentanyl is delivered over the delivery period.

6. The method of claim 1, wherein the donor reservoir formulation comprising a fentanyl salt is placed in contact with the body surface.

7. The method of claim 6, wherein the fentanyl salt comprises about 1.9 to 2.0 wt % of the formulation.

Analysis

The Examiner states that the conflicting claims are not patentably distinct “because claim 1 of the current application recites a method of drug delivery where in the concentration is maintained above about 16 mM which from appellant’s specification is a composition that comprises about 1-2% fentanyl (see appellant's specification page 29) which is also the same composition as claim 7” of the Southam patent (Ans. 16). Thus, the Examiner contends that instant claim 1 is a broader version of claim 1 of the Southam patent (Ans. 16-17).

Appellant argues that the Southam claims “do not lead to any understanding that when the final additional dose is applied, the concentration of fentanyl salt remaining in the donor reservoir must be above about 16 mM” (App. Br. 35).

We are not convinced by this argument that the Examiner erred. Instant claim 1 requires that the concentration of fentanyl salt in the device is “above 16 mM . . . substantially throughout the . . . [drug] delivery period”, but does not state the delivery period. Claim 1 of Southam has an upper limit for a delivery period, but not a lower limit; patented claim 2 is directed to a delivery period of about 5 to 15 minutes. Thus, when the concentration in the Southam delivery is above 16 mM for about 5 minutes – all the limitations of claim instant 1 are met.

Appellant also argues that claim 7 specifying “about 1.9 to 2.0 wt % of the formulation” does not “not specify how much formulation is present and it is certainly possible that the amount of formulation could be present so that the when the final dose is administered, the concentration of fentanyl is below the level recited in the claims on appeal” (App. Br. 35). Appellant states that “[t]o take the position that the amount of formulation should be selected such that when the amount of fentanyl salt is 1.9 to 2.0 wt % and when the quantity per dose and total number of doses are selected so that the remaining fentanyl concentration meets that defined in the claims on appeal would be to again rely on an ‘obvious to try’ standard” (App. Br. 35).

This argument is not persuasive. As discussed above, when the final dosage is delivered within a delivery period of about 5 to 15 minutes, the limitations of instant claim 1 are met. The amount of fentanyl recited in claim 7 is a concentration (in wt %) as is the amount (16 mM) required by instant claim 1. Appellant has not presented any evidence that the concentration of fentanyl in claim 7 is less than the amount required by claim 1.

Appeal 2007-1556
Application 08/463,904

For the foregoing reasons, we affirm the rejection of claim 1. Claims 4-7 and 9 fall with claim 1 because separate reasons for their patentability were not provided. 37 C.F.R. § 41.37(c)(1)(vii).

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

Ssc:

DIEHL SERVILLA LLC
77 BRANT AVENUE
SUITE 210
CLARK, NJ 07066